

88586

Access DB#

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Mike Mellow Examiner #: 69404 Date: 3/7/03  
 Art Unit: 1654 Phone Number 30 8-4230 Serial Number: 09/937506  
 Mail Box and Bldg/Room Location: CU1 Results Format Preferred (circle): PAPER DISK E-MAIL  
10 A03

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*  
 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Association of no-synthase inhibitors  
 Inventors (please provide full names): Michel August, Jeremiah Harnett,  
Pierre-Etienne Chabir de Lassauniere  
 Earliest Priority Filing Date: 2/4/99

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

*highlighted* Please search the <sup>if no</sup> hits  
compounds together and then  
 search them separately and see  
 if there is any common  
use of them separately.

thanks.

Mary Jane Ruhl  
 Tech. Info. Specialist, STIC  
 TC-1600  
 CM-1, Room 6A-06  
 Phone: 605-1155

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## STAFF USE ONLY

Searcher: \_\_\_\_\_  
 Searcher Phone #: \_\_\_\_\_  
 Searcher Location: \_\_\_\_\_  
 Date Searcher Picked Up: 3/10/03  
 Date Completed: 3/11/03  
 Searcher Prep & Review Time: 12  
 Clerical Prep Time: \_\_\_\_\_  
 Online Time: 120

## Type of Search

NA Sequence (#) \_\_\_\_\_  
 AA Sequence (#) \_\_\_\_\_  
 Structure (#) \_\_\_\_\_  
 Bibliographic \_\_\_\_\_  
 Litigation \_\_\_\_\_  
 Fulltext \_\_\_\_\_  
 Patent Family \_\_\_\_\_  
 Other \_\_\_\_\_

## Vendors and cost where applicable

STN \_\_\_\_\_  
 Dialog \_\_\_\_\_  
 Questel/Orbit \_\_\_\_\_  
 Dr. Link \_\_\_\_\_  
 Lexis/Nexis \_\_\_\_\_  
 Sequence Systems \_\_\_\_\_  
 WWW/Internet \_\_\_\_\_  
 Other (specify) \_\_\_\_\_

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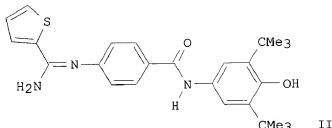
Meller 09/937,306

10/03/2003

=> d ibib abs hitstr 1-3

L8 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2002:6386 HCAPLUS  
 DOCUMENT NUMBER: 136:69731  
 TITLE: Preparation of N-phenylthiophenecarboxamidines and analogs as NO synthase and lipid peroxidation inhibitors  
 INVENTOR(S): Chabrier de Lassauniere, Pierre Etienne; Auvin, Serge; Bigg, Dennis; Auguet, Michel; Harnett, Jeremiah  
 PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S.), Fr.  
 SOURCE: U.S., 63 pp., Cont.-in-part of U. S. Ser. No. 381,749. CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6335445	B1	20020101	US 1999-456205	19991207
FR 2761066	A1	19980925	FR 1997-3528	19970324
FR 2761066	B1	20001124		
FR 2764889	A1	19981224	FR 1997-7701	19970620
FR 2764889	B1	20000901		
WO 9842696	A1	19981001	WO 1998-FR288	19980216
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, CA, GN, ML, MR, NE, SN, TD, TG			
US 6340700	B1	20020122	US 1999-381749	19990922
US 2002007062	A1	20020117	US 2001-882264	20010615
US 2002045753	A1	20020418	US 2001-945782	20010904
US 2002042511	A1	20020411	US 2001-953682	20010917
PRIORITY APPLN. INFO.:			FR 1997-3528	A 19970324
			FR 1997-7701	A 19970620
			WO 1998-FR288	W 19980216
			US 1999-381749	A2 19990922
			WO 1998-FR1250	W 19980615
			US 1999-456205	A3 19991207
			US 2001-882264	A3 20010615
OTHER SOURCE(S):		MARPAT 136:69731		
GI				



AB RZ21Z2Z3N:C(NH2)R1 [I; R = H, (un)substituted C6H4OR3, indolyl, etc.; R1 = alkyl or (un)substituted (hetero)aryl; R3 = H, alkyl, etc.; Z = bond, CO, alkylene(carbonyl), CONH, etc.; Z1 = bond or heterocyclylene; Z2 = bond, alkylene(oxy), etc.; Z3 = (un)substituted phenylene] were prepd. Thus, 4-(O2N)C6H4NH2 was amidated by 3,5-di-tert-butyl-4-hydroxybenzoic acid and the reduced product amidated by S-methyl-2-thiophenethiocarboximide hydroiodide to give title compd. II. Data for biol. activity of I were given.

IT 125978-95-2, NO synthase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (mediated disorders; treatment; prepn. of N-phenylthiophenecarboxamides and analogs as NO synthase and lipid peroxid. inhibitors)

RN 125978-95-2 HCAPLUS

CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:725626 HCAPLUS

DOCUMENT NUMBER: 133:281650

TITLE: Novel lipoic acid derivatives, their preparation, and

pharmaceutical compositions containing them

INVENTOR(S): Harnett, Jeremiah; Auguet, Michel;

Chabrier, De Lassauniere Pierre-etienne

PATENT ASSIGNEE(S): Societe De Conseil de Recherches et d'applications

Scientifiques (S.C.R.A.S., Fr.; Chabrier De

Lassauniere, Pierre-Etienne

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059899	A1	20001012	WO 2000-FR814	20000331
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,			

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 FR 2791677 A1 20001006 FR 1999-4132 19990402  
 FR 2791677 B1 20010817  
 FR 2805537 A1 20010831 FR 2000-2315 20000224  
 EP 1169316 A1 20020109 EP 2000-918930 20000331  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 JP 2003505341 T2 20030212 JP 2000-609410 20000331  
 PRIORITY APPLN. INFO.: FR 1999-4132 A 19990402  
 FR 2000-2315 A 20000224  
 WO 2000-FR814 W 20000331

OTHER SOURCE(S): MARPAT 133:281650  
 GI



- AB The invention concerns novel lipoic acid derivs. I [A = (CH<sub>2</sub>)mNR3CO(CH<sub>2</sub>)n, (CH<sub>2</sub>)mCONR3(CH<sub>2</sub>)n, (CH<sub>2</sub>)mNR3(CH<sub>2</sub>)n, (CH<sub>2</sub>)mCONR3(CH<sub>2</sub>)pCONR4(CH<sub>2</sub>)n, (CH<sub>2</sub>)mNR3CONR4(CH<sub>2</sub>)n, (CH<sub>2</sub>)mNR3CONR4(CH<sub>2</sub>)m; R1, R2, R3, R4 = H, linear or branched C1-6-alkyl; X = X1, (CH<sub>2</sub>)q; Y = N:C(B)NH<sub>2</sub>, Y1; R5 = H, C1-6-alkyl, (CH<sub>2</sub>)mQ; T = (CH<sub>2</sub>)1Y; Q = halogen, OH, CN, NH<sub>2</sub>, alkoxy, alkylthio, (di)alkylamino, 5- or 6-membered heterocycle contg. O, NR6, S; R6 = H, C1-6-alkyl; R7 = H, C1-6-alkyl; B = NR8R9, SR10; R8, R9 = H, linear or branched C1-6-alkyl, NO<sub>2</sub>; R10 = H, linear or branched C1-6-alkyl; i = 0 - 6; m, n = 0 - 6; p = 2 - 6; q = 0 - 6] and II (A, X, Y, R1, R2 as in I), which have an inhibiting action with respect to NO-synthase enzymes producing nitrogen monoxide NO and/or are agents enabling the regeneration of antioxidants or entities trapping reactive oxygen species (ROS) and intervening in a more general manner in the redox status of thiol groups. Thus, I [3-AXY = (CH<sub>2</sub>)4CONHC6H4(NHC(2-thienyl)NH)-4] was prepd. from thioctic acid via amidation with N-Boc-L,4-phenylenediamine, followed by deprotection and condensation with S-methyl-2-thiophenethiocarboximide. I showed NO synthase inhibition (CI<sub>50</sub> = 4.5 .mu.M) and oxidative stress protection (CE<sub>50</sub> = 30.mu.M).
- IT 125978-95-2, NO synthase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (prepn. of novel lipoic acid derivs. with NO synthase inhibition activity and pharmaceutical compns. contg. them)
- RN 125978-95-2 HCAPLUS  
 CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

- IT 10102-43-9, Nitrogen monoxide, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (prepn. of novel lipoic acid derivs. with NO synthase inhibition activity and pharmaceutical compns. contg. them)
- RN 10102-43-9 HCAPLUS  
 CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N=O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2000:725417 HCAPLUS  
 DOCUMENT NUMBER: 133:276363  
 TITLE: Association of NO-synthase inhibitors and metabolic antioxidants  
 INVENTOR(S): Auguet, Michel; Harnett, Jeremiah; Chabrier De Lassauniere, Pierre-etienne  
 PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.  
 SOURCE: PCT Int. Appl., 16 pp.  
 CODEN: P1XXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059448	A2	20001012	WO 2000-FR812	20000331
WO 2000059448	A3	20010308		
W:				
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, BU, CA, CH, CN, CO, CR, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2791571	A1	20001006	FR 1999-4134	19990402
FR 2791571	B1	20021004		
EP 1169005	A2	20020109	EP 2000-915262	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001004770	A	20011123	NO 2001-4770	20011001
PRIORITY APPLN. INFO.:			FR 1999-4134	A 19990402
			WO 2000-FR812	W 20000331
AB				
The invention relates to a pharmaceutical compn. comprising as an active ingredient one or several substances interfering with the synthesis of nitrogen monoxide by inhibiting NO-synthase and one or several metabolic antioxidants contg. thiol groups and intervening in the redox status of the thiol groups, and optionally a pharmaceutically acceptable support. The invention also relates to a product contg. one or several NO-synthase inhibitors and one or several metabolic antioxidants intervening in the redox status of the thiol groups, as a combined product in a sepd. form of said active ingredients. A mixt. of 3 mg/kg N-phenyl-2-thiophenecarboximidamide and 10 mg/kg lipoic acid increased the dopamine level in guinea pigs suffering from parkinson to 5.21 ng/mg nervous tissue which was higher than either compds.				
IT				
52-67-5D, Penicillamine, dimeric derivs. 74-79-3, L Arginine, biological studies 79-17-4, Aminoguanidine 306-60-5, Agmatine 616-91-1 1098-97-1, Pyritinol 2149-70-4, Nitroarginine 2214-67-7				

2942-42-9, 7 Nitroindazole 2986-20-1, s-Ethylisothiurea  
 3483-12-3, Dithiothreitol 3737-39-1 5401-94-5,  
 5 Nitroindazole 7597-18-4, 6 Nitroindazole 17035-90-4  
 22780-54-7, 2-Iminopiperidine 25371-96-4,  
 1,2-(Trifluoromethylphenyl)imidazole 50903-99-6  
 57828-26-9, Lipoic acid 57828-26-9D, Lipoic acid,  
 derivs. 156719-41-4, S-Methyl-L-thiocitrulline  
 158875-72-0, S-Ethyl-L-thiocitrulline 171082-82-9  
 179555-23-8 194245-33-5 300357-99-7  
 300358-00-3

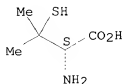
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(assocn. of NO-synthase inhibitors and metabolic antioxidants)

RN 52-67-5 HCAPLUS

CN D-Valine, 3-mercapto- (9CI) (CA INDEX NAME)

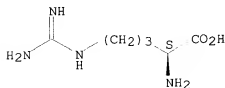
Absolute stereochemistry.



RN 74-79-3 HCAPLUS

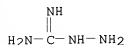
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



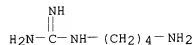
RN 79-17-4 HCAPLUS

CN Hydrazinecarboximidamide (9CI) (CA INDEX NAME)



RN 306-60-5 HCAPLUS

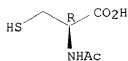
CN Guanidine, (4-aminobutyl)- (8CI, 9CI) (CA INDEX NAME)



RN 616-91-1 HCAPLUS

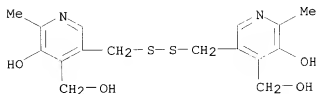
CN L-Cysteine, N-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 1098-97-1 HCAPLUS

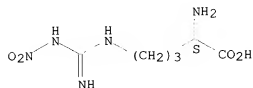
CN 4-Pyridinemethanol, 3,3'-[dithiobis(methylene)]bis[5-hydroxy-6-methyl- (9CI) (CA INDEX NAME)



RN 2149-70-4 HCAPLUS

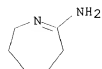
CN L-Ornithine, N5-[imino(nitroamino)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



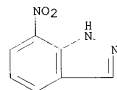
RN 2214-67-7 HCAPLUS

CN 2H-Azepin-7-amine, 3,4,5,6-tetrahydro- (9CI) (CA INDEX NAME)



RN 2942-42-9 HCAPLUS

CN 1H-Indazole, 7-nitro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 2986-20-1 HCAPLUS

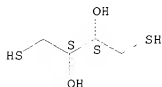
CN Carbamimidothioic acid, ethyl ester (9CI) (CA INDEX NAME)



RN 3483-12-3 HCAPLUS

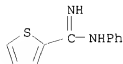
CN 2,3-Butanediol, 1,4-dimercapto-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



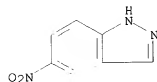
RN 3737-39-1 HCAPLUS

CN 2-Thiophenecarboximidamide, N-phenyl- (9CI) (CA INDEX NAME)



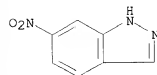
RN 5401-94-5 HCAPLUS

CN 1H-Indazole, 5-nitro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 7597-18-4 HCAPLUS

CN 1H-Indazole, 6-nitro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

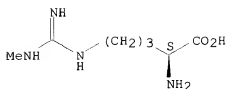


RN 17035-90-4 HCAPLUS

CN L-Ornithine, N5-[imino(methylamino)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

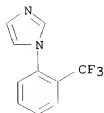




RN 22780-54-7 HCAPLUS  
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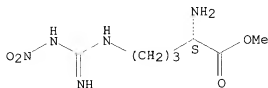


RN 25371-96-4 HCAPLUS  
 CN 1H-Imidazole, 1-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 50903-99-6 HCAPLUS  
 CN L-Ornithine, N5-[imino(nitroamino)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 57828-26-9 HCAPLUS  
 CN Lipoic acid (9CI) (CA INDEX NAME)

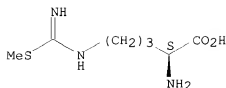
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 57828-26-9 HCAPLUS  
 CN Lipoic acid (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 156719-41-4 HCAPLUS  
 CN L-Ornithine, N5-[imino(methylthio)methyl]- (9CI) (CA INDEX NAME)

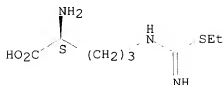
Absolute stereochemistry. Rotation (+).



RN 158875-72-0 HCAPLUS

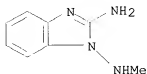
CN L-Ornithine, N5-[(ethylthio)iminomethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



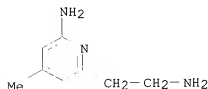
RN 171082-82-9 HCAPLUS

CN 1H-Benzimidazole-1,2-diamine, N1-methyl- (9CI) (CA INDEX NAME)



RN 179555-23-8 HCAPLUS

CN 2-Pyridineethanamine, 6-amino-4-methyl- (9CI) (CA INDEX NAME)



RN 194245-33-5 HCAPLUS

CN 2-Pyrimidinamine, 1,4-dihydro- (9CI) (CA INDEX NAME)



RN 300357-99-7 HCAPLUS

CN 2H-1,3-Thiazin-2-imine, 5,6-dihydro- (9CI) (CA INDEX NAME)

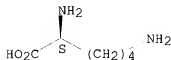


RN 300358-00-3 HCAPLUS  
CN 2H-1,3-Oxazin-2-imine, 5,6-dihydro- (9CI) (CA INDEX NAME)



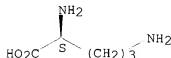
IT 56-87-1, Lysine, biological studies 70-26-8, Ornithine  
10102-43-9, Nitrogen monoxide, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(assocn. of NO-synthase inhibitors and metabolic antioxidants)  
RN 56-87-1 HCAPLUS  
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70-26-8 HCAPLUS  
CN L-Ornithine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10102-43-9 HCAPLUS  
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N=O

IT 125978-95-2, NO-synthase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; assocn. of NO-synthase inhibitors and metabolic  
antioxidants)  
RN 125978-95-2 HCAPLUS  
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*